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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/916,709	07/27/2001	Michael D. Doyle	001-1	8247

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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 02/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/916,709	DOYLE ET AL.	
	Examiner	Art Unit	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7 and 9-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-7, and 9-11* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendments and remarks, filed 12/01/05, are acknowledged. Amended claims 1-4, 6-7, and 9-11 are acknowledged.

Applicants' arguments, filed 12/01/05, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-4, 6-7, and 9-11 are herein under examination.

Claim Objections

Claim 4 is objected to because of the following informalities: Claim 4 (line 28) misspells the word "superimpos". Claim 4 (line 29) misspells the word "gri" and recites the phrase "the a" which is confusing grammar. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

NEW MATTER

Applicants do not point to any area of support in the originally filed application for the amendments. There does not appear to be adequate written description for the phrase "volume image data indicated by the code assigned to the coded micro dissected section sample" (last two lines in claim 1). While there is support for using index data to superimpose gene expression data and image data (original claim 4), there does not appear to be adequate written support that the volume image data is indicated by the code. In addition, there does not appear to be adequate written description for the phrase "superimpos[sic] gene expression data of a micro dissected section sample gri[sic] onto the a [sic] spatial coordinate [...] indicated by the code of the coded micro dissected section sample holder holding the micro dissected section sample" in claim 4 (lines 28-31). Because the introduction of these phrases do not appear to have adequate written support in the originally filed specification, claims, and/or drawings, these amendments are considered to be NEW MATTER. Claims 2-3 and 6 are also rejected due to their dependency from instant claims 1 and 4. This rejection is necessitated by amendment.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6-7, and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 1 (line 9), 4 (line 12), 7 (line 7), and 11 (line 7) recite the phrase "unattendedly micro dissecting" which is vague and indefinite. It is unclear what Applicant means by this phrase. It is unclear by what or by whom the micro dissecting is being unattended. Clarification of this issue via clearer claim wording is requested. Claims 2-3, 6, and 9-10 are also rejected due to their dependency from claims 1, 4, and 7. This rejection is necessitated by amendment.

Claim 4 (lines 28-29) recite the phrase "superimpose[sic] gene expression data of a micro dissected section sample gri[sic] onto the a [sic] spatial coordinate" which is vague and indefinite. It is unclear if the expression data of a grid is intended to be superimposed on a previously mentioned coordinate or on any coordinate. Clarification of this issue via clearer claim wording is requested. Claim 6 is also rejected due to its dependency from claim 4. This rejection is necessitated by amendment.

Claims 7 (line 5), 9 (line 4), 10 (last line), and 11 (line 6) recite the phrase "based on" which is vague and indefinite. It is unclear what criteria and to what degree these criteria must be met to be considered to be "based on". Clarification of this issue via clearer claim wording is requested. This rejection is maintained.

Applicants removed this phrase from claim 1, but it is still present in claims 7, 9, 10, and 11.

Claims 9 and 10 recite limitations "each coded micro dissected section sample"; however, these claims are confusing as it is unclear which steps in instant claim 7 (from which they depend) they are intended to further limit. Clarification of this issue via clearer claim wording is requested. This rejection is necessitated by amendment.

Applicants state they have deleted or clarified this rejection; however, the amendment still does not clarify these claims, therefore the rejection is maintained.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. (e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 6-7, and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heppelmann et al. (Journal of Microscopy, Vol. 156, Pt. 2, 1989, pages 163-172) in view of Cole et al. (Nature Genetics supplement, Vol. 21, 1999, pages 38-41), Farr et al. (P/N 5,811,231), Emmert-Buck et al. (Science, Vol. 274, 1996, pages 998-1001), and Lemelson (P/N 6,058,323).

This rejection is necessitated by amendment.

Heppelmann et al. describe methods for creating multidimensional morphological reconstruction of biological tissue data characterizing a biological tissue sample by cutting histologically thin sections of tissue in two sets of alternating serial sample sections (page 163, lines 1-12) as stated in claims 1, 4, 7, and 11. Heppelmann et al. describe performing these three dimensional reconstructions with graphical techniques and computer-aided methods (page 163, lines 13-14) featuring a spatial matrix of image data with x, y, and z axes as seen in Figure 4, which represents mapping image data obtained from the first set of alternating serial sections onto a coordinate system as well as volume image data correspondence, as stated in claims 1, 4, 7, and 9-11. Heppelmann et al. describe cutting the second set of sections (for ultrastructural examination) with an ultracut ultramicrotome and mounting them on single-slot grids to be further examined (page 164, last paragraph) which represents microdissecting each serial section to create a set of microdissected section samples for each serial section of the second set, as stated in claims 1, 4, 7, and 11. Heppelmann et al. describe examined 3-D structures were fitted and projected onto the lines of a coordinate system of the z-dimension according to their vertical position which was calculated from the section thickness as well as connecting the same

structures in their vertical projection revealed in a side view projection diagram (page 165, third paragraph and Figure 2) which represents assigning a unique code (calculation) to each section sample indicating tissue space coordinates and specific range in the morphological space matrix, as stated in instant claims 1, 7, 9, 10, and 11. Heppelmann et al. describe the sections were mounted in sequence on mesh grids (page 165, lines 12-14) which is reasonably interpreted to be associating each incised section sample with unique set of indices as the mesh grids have x and y coordinates, with each individual sample placed in a known location. Heppelmann et al. describe histologically-staining the first set of sections and adding a coverslip (page 164, fifth paragraph) which could be used for light microscopy reconstructions (page 163, lines 4-5) as stated in claim 4. Heppelmann et al. describe that the second set of tissue sections are covered with a synthetic membrane which is then further cut (page 164, paragraphs 6 and 7), as stated in claim 4.

Heppelmann et al. do not teach using a microarray and biological data analyses type which involve mRNA as elected in the species elections. Heppelmann et al. do not teach linking these data to each coded microdissected tissue sample in the multidimensional morphological matrix. Heppelmann et al. do not describe unattendedly microdissecting, analyzing tissue with monoclonal antibodies, obtaining gene expression data, and superimposing them on the multidimensional morphological matrix of image data to display correlating values of data with corresponding locations on the matrix.

Cole et al. describe a web-based, visual system for allowing querying of gene expression profiles while viewing associated anatomy and histopathology (page 40, col. 2 (third paragraph) which represents a system of creating morphological reconstruction of biological data

characterizing a tissue, as stated in instant claims 7 and 11. Cole et al. describe a model for integrating three dimensional expression data obtained using a microarray involving mRNA analysis (page 38, abstract (lines 5-6), and col. 1 (lines 1-4)) which represents methods and systems for analyzing sections providing a plurality of biological characteristics of the coded micro-dissected samples, as stated in instant claims 1, 3, 7, and 11. Cole et al. discuss cutting tissue in transverse cross-sections (representing X and Y dimensions) available for micro-dissection and recutting adjacent serial sections in the Z dimension (page 40, col. 1, lines 7-14) which are used to create a multidimensional morphological spatial matrix of image data as seen in Figure 1 including letters A – G for different sections which represents micro-dissecting across each serial section of a set with uniquely coded (lettered) sections, as stated in instant claims 1, 4, 7, 9, and 11. Cole et al. describe the transverse sections have been annotated with the types and location of histopathology present (Figure 1 caption) wherein the annotation for the sections represent uniquely coded sections. Cole et al. discuss the placement of tissue on slides (page 40, col. 1, lines 11-12) and other newly developed fixation and embedding strategies (page 39, col. 2, lines 15-16). Cole et al. describe methods of preparing microarrays from micro-dissected cells (page 40, col. 1, lines 19-25 and 37-39). Cole et al. discuss that the above processes allows for the determination of exact physical relationships between morphological data (one set) on which to overlay gene expression data (second set)(page 40, col. 1, lines 14-17 and col. 2, lines 16-24) as well as annotation on tissue sections (Figure 1 and its caption) which represent superimposing biological data of the micro-dissected section sample upon volume image data indicated by code assigned to the sample of the morphological tissue space matrix, as well as obtaining and analyzing biological data, and linking data characterizing each sample to

the location, as stated in claims 1, 4, 7, and 11. Cole et al. describe viewing this information on computers and displaying a data chart in three dimensions (page 40, col. 2, lines 26-38) which represent spatially mapping the biological data characterizing each micro-dissected section sample of the second set onto the multidimensional morphological tissue space matrix from the first set, as stated in claim 1. Cole et al. show images of stained tissue sample sections obtained from light microscopy (Figure 1, molecular view) as stated in claim 4. Cole et al. do not teach unattendedly microdissecting, superimposing analyzed RNA data on the multidimensional morphological matrix of image data, analyzing tissue with monoclonal antibodies, and correlating data with corresponding locations on the matrix.

Farr et al. describe a method of measuring biological data, particularly as gene expression levels from specific organs of animal tissues to characterize and identify cellular and subcellular effects of potential toxins on an animal cell (col. 2, lines 52-62 and col. 6, lines 15-23). Farr et al. describe starting experiments with tissue sample and cell lines (col. 6, lines 15-23). Farr et al. describe the results graphically in Figures 1-11 (col. 31, lines 5-6) which consist of multidimensional (3D) representations of the biological data. As can be seen in the Figures 1-11, each data column is indexed and to a particular set of conditions, such as the expression of an enzyme under control of different promoters in the presence of varying concentrations of a test compound (col. 3, lines 24-67). Each of these particular set of conditions was tested with genetic material bound to a solid support membrane which was placed on a 96-well plate referring to rows and columns (col. 20, lines 53-67; col. 26, lines 9-11; and col. 29, line 49 to col. 30, line 31) which represents coded micro-dissected section sample holders which allowed for proper coding and correlation of each set of test conditions to the resulting graphical representations

described above, as stated in claims 1, 4, and 6. Farr et al. describe an autoradiograph taped to a 96-well plate holder to align the radioactive dots with the holes of the plate holder so that each well is quantified according it each well position (col. 28, lines 23-27 and col. 29, line 49 to col. 30, line 31) which is a form of image data superimposed and visually transferring of grid elements to the corresponding sample holder, providing sample holders indicating identity of the sample sections and coordinate location, and analyzing each grid element with expression data, as stated in instant claims 1 and 4. Farr et al. describe correlating the results and creating profiles (col. 28, lines 30-32) as stated in claim 6. Farr et al. describe analyzing assays using antibodies to detect proteins (col. 19, lines 55-67 and col. 20, lines 1-14) with expression levels being regulated by interactions between surface receptors and ligands (col. 4, lines 52-55) as stated in claim 2. Farr et al. describe the method to include detecting levels of mRNA (col. 20, lines 25-67) as stated in claim 3. Farr et al. do not teach unattendedly microdissecting or physically transferring incised grid elements.

Emmert-Buck et al. describe a film or membrane applied to the surface of a tissue section on a glass slide (abstract, lines 3-5), which represents mounting and covering a second set of sections with a micro dissection membrane, as stated in instant claim 4. Emmert-Buck et al. describe automatic microdissection without manual procedure and a laser applied to specific locations of the film to procure specifically targeted cells that can then be transferred (page 998, third column, first full paragraph and abstract, lines 5-9) which represents unattendedly microdissecting and suggests transferring specific micro-dissected tissue and selecting only particular subsections.

Lemelson describes the idea of generating images of tissue which may be computer processed and analyzed to generate multiple cross-sectional views such as parallel slice images with code signals indicating coordinate locations of those structures (col. 9, third paragraph) which represents assigning a unique code to tissue sections indicating tissue space coordinates, as stated in instant claims 1, 4, 7, and 11. Lemelson does not describe the coded microdissected section holders.

Cole et al. state that gene expression microarrays hold great promise in studies of human disease states (abstract, line 1). While some technical issues have yet to be addressed, other precise measurement techniques are at hand to view molecular anatomy of normal cells and their disease counterparts (Cole et al., abstract). Farr et al. state the need for quick, inexpensive and reliable alternatives to toxicity testing in animals (col. 2, lines 11-13) such as using techniques of measuring transcription and translation levels of genes (col. 2, lines 52-62). Farr et al. state the kits and methods of their invention yield rapid and direct information about the nature of a compound's action on mammalian cells (col. 3, lines 12-21). Farr et al. also state that the basic construction of the kits, processes, and products of their invention can be altered to provide other embodiments (col. 32, lines 14-21). Heppelmann et al. state that complex morphological structures cannot be fully appreciated without three-dimensional reconstruction (page 163, lines 15-16). Heppelmann et al. point out that stacking of contoured sections for reconstruction is an old technique that is now aided by graphical methods and computers (page 163, lines 16-21).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to utilize improved methods of comparison of multidimensional graphic data expression representation to microscopy data, as stated by Cole et al. (page 40, col. 2, lines 21-

28) via three-dimensional histological techniques to increase understanding of complex morphological structures as stated by Heppelmann et al. (page 163, lines 15-16 and page 171, lines 11-13), using simple and precision tissue extraction with laser capture microdissection that minimizes contamination, as stated by Emmert-Buck (abstract and page 998, col. 3, lines 2-6 and 12-15), and displaying the gene expression data in easy-to-read uniquely coded tissue sections, slides, and three-dimensional graphs as shown by Farr et al. (such as Figure 1) and Lemelson, because these rapid, exact and efficient techniques would improve accuracy and visual representation for easy interpretation of correlations between the data types available to scientists at the time of the invention (Emmert-Buck, abstract; Farr et al., col. 2, lines 11-13; Cole et al., abstract and page 38, col. 1, first paragraph).

The person of ordinary skill in the art at the time the invention was made would have been motivated to study complex 3-D morphological structures of Heppelmann et al. (page 163, fifth paragraph) combined with the entire tissue studies including gene expression profiles of the different sections, as stated by Cole et al. in order to discover genotypic changes in tissue that may not be apparent phenotypically to provide new insights in cancer biology at the molecular level (Cole et al., page 38, col. 1, first paragraph and page 38, col. 2, second paragraph).

The person of ordinary skill in the art at the time the invention was made would have been motivated to discover genotypic changes in tissue sections from Heppelmann et al. and Cole et al. via coded microarray plates of Farr et al. (col. 29, lines 49 to col. 30, line 31) in order to organize, interpret, and gain insights from large amounts of gene expression data generated by complex biological systems, as stated by Cole et al. (page 38, col. 1, first paragraph), and to

precisely identify and characterize biological effects on certain tissues, as stated by Farr et al. (abstract, lines 1-12).

The person of ordinary skill in the art at the time the invention was made would have been motivated to create tissue sections of Heppelmann et al., Cole et al., and Farr et al. with the automated laser capture microdissection as stated by Emmert-Buck et al. in order to provide a ease, precision, and efficiency in a rapid one-step procurement of selected targeted human cells from a section of complex, heterogenous tissue (Emmert-Buck et al. abstract and page 998, col. 2, second paragraph).

The person of ordinary skill in the art at the time the invention was made would have been motivated to analyze tissue sample sections of Heppelmann et al., Cole et al., Farr et al., Emmert-Buck with the computerized imaging system with cross sectional tissue views indicating coordinate locations of the structures of Lemelson (col. 9, third paragraph) in order to efficiently query gene expression profiles while viewing associated anatomy and histopathology which will further understanding of molecular events that underlie tumor development for producing new diagnostic, prognostic, and therapeutic targets for the benefits of patients (Cole et al., page 40, col. 2, third and fourth paragraphs).

One of ordinary skill in the art would have expected success of combining the three-dimensional reconstruction techniques of Heppelman et al. with Cole et al.'s visual system for allowing query of gene expression profiles while viewing associated anatomy and histopathology because both involve a variety of tissue sectioning methodologies for three dimensional reconstructions (Heppelmann et al., summary; Cole et al., page 39, col. 2, last paragraph).

One of ordinary skill in the art would have expected success of combining the tissue section analyses of Cole et al. with the tissue analyses of Farr et al. because both use microarrays for gene expression analyses which allows a quick and expensive alternatives to toxicity testing in animals (Farr et al., col. 2, first paragraph).

One of ordinary skill in the art would have expected success of combining the laser capture microdissection technique of Emmert-Buck et al. with the tissue samples of Farr et al. because Emmert-Buck emphasizes the next generation of molecular analysis methods involving tissue selection need to be miniaturized and automated for clinical molecular diagnostic testing of gene expression (Emmert-Buck, page 998, col. 1, first paragraph and abstract), such as the gene expressions studied by Farr et al.

One of ordinary skill in the art would have expected success of combining the computer image analysis with coordinate locations of Lemelson with the visually oriented system of Cole et al. as both use the coordinate locations to orient views to the anatomic location, such as tumors, which allows for a rapid query of profiles across a spectrum of samples as stated in Cole et al. (Figure 1).

Thus, Heppelmann et al., in view of Cole et al., Farr et al., Emmert-Buck et al., and Lemelson, make obvious and motivate the limitations of claims 1-3, 6-7, and 9-11.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heppelmann et al. (Journal of Microscopy, Vol. 156, Pt. 2, 1989, pages 163-172) in view of Cole et al. (Nature Genetics supplement, Vol. 21, 1999, pages 38-41), Farr et al. (P/N 5,811,231), Emmert-Buck et al. (Science, Vol. 274, 1996, pages 998-1001), and Lemelson (P/N 6,058,323) as applied to claims 1-3, 6-7, and 9-11 above, and further in view of Bogen et al. (P/N 6,281004).

Heppelmann et al., in view of Cole et al., Farr et al., Emmert-Buck et al., and Lemelson, make obvious and motivate the limitations of claims 1-3, 6-7, and 9-11, as described in the 35 USC 103 rejection above. These references do not describe coded micro-dissected section holders.

Bogen et al. describe microscope slides with tissue sections containing labels containing surgical accession number, patient name, and a barcode (col. 7, last paragraph) which represents a coded tissue section sample holder, as stated in instant claim 4.

The person of ordinary skill in the art at the time the invention was made would have been motivated to code tissue sample sections of Heppelmann et al., Cole et al., Farr et al., Emmert-Buck, and Lemelson with a coded tissue section sample holder of Bogen et al. (col. 7, last paragraph) in order to efficiently compare and contrast large datasets across multiple patients and samples, as stated by Cole et al. (page 40, col. 2, third paragraph).

One of ordinary skill in the art would have expected success of combining the coded tissue sample holder with the tissue sections of Bogen et al. with the tissue sections of Heppelmann et al., in view of Cole et al., Farr et al., Emmert-Buck et al., and Lemelson as it would reliably monitor quality control within the laboratories to ensure accuracy, as stated by Bogen et al. (col. 1, first paragraph).

Thus, Heppelmann et al., in view of Cole et al., Farr et al., Emmert-Buck et al., and Lemelson, and Bogen et al., make obvious and motivate the instant invention. This rejection is necessitated by amendment.

Applicants summarize their invention. Applicants summarize the Heppelmann et al., Cole et al., Farr et al. and Emmert-Buck references. Applicants argue that none of the references disclose the steps recited in claims 1, 4, 7, and 11, including unattendedly micro-dissecting each serial sample, assigning code, analyzing the sample, and superimposing or linking the biological data. This statement is found unpersuasive as Heppelman et al. recite micro-dissecting serial samples and Emmert-Buck et al. recite steps including unattendedly micro-dissecting samples (see rejection above). Lemelson and Bogen et al. (newly cited references due to the new claim amendments) recite steps of assigning code (see rejection above). Cole et al. recite steps of analyzing a sample (see rejection above). Cole et al. and Farr et al. recite steps of superimposing or linking biological data (see rejection above). It is noted that not all limitations of the instant claims come from a single reference which is why this is a 35 USC 103 rejection, and not a 35 USC 102 rejection. Applicants argue that the re-embedding technique of Heppelmann et al., Cole et al., and Emmert-Buck has a fundamental principal of operation that involves selecting an area of interest from a section to be further analyzed whereas the instant invention involves unattendedly micro-dissection without any selection by the investigator. This statement is found unpersuasive as Emmert-Buck et al. describe automatic micro-dissection without manual

procedure (page 998, third column, first full paragraph and abstract) which broadly and reasonably represents unattended procedure. It is noted that the instant claims do not recite micro-dissection "without any selection by an investigator". Applicants argue that the proposed combination would change the principle operation of the primary reference and render it inoperable. In particular, Applicants argue that if the serial section of Heppelmann were micro-dissected into a grid pattern, it could not be used for the next step of ultrastructural analysis since the structure of the serial section would have been destroyed. This statement is found unpersuasive as Heppelmann et al. describe further ultrastructural examination (page 164, last paragraph). It is also noted that the instant claims list steps, but not that these steps must be followed in a particular order. Applicants' arguments are deemed unpersuasive for the reasons given above.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

MARJORIE A. MORAN
PRIMARY EXAMINER
Marjorie A. Moran
2/21/06

February 14, 2006